

SEQUENCE LISTING

<110> Jensen, Michael

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Modified Cells

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<223> Human Wild-type Inosine Monophosphate Dehydrogenase
II (IMPDH II)

<300>

<301> Collart, F.R. and Huberman, E.

<302> Cloning and sequence analysis of the human and

<303> J. Biol. Chem. (1988)

<304> 263

<306> 15769-15772

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<301> Farazi et al.
<303> J. Biol. Chem. (1997)
<304> 271

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 Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro
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 Lys Tyr Arg Leu Asp Leu Leu Ala Gln Ala Gly Val Asp Val Val Val
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 Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Gly Ile Gln
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 Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala Val Gln
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 Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala Gly Ile
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<300>
 <301> Farazi et al.
 <303> J. Biol. Chem. (1997)
 <304> 272
 <305> 2
 <306> 961-965

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Gln	Ala	Asn	Glu	Val		Lys	Val	Lys	Lys	Tyr	Glu	Gln	Gly	Phe	Ile															
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Glu	Ala	Lys	Ala	Arg	His	Gly	Phe	Cys	Gly	Ile	Pro	Ile	Thr	Asp	Thr															
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	245					250					255																			
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Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly Glu Tyr Phe Phe Ser
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440 445 450

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Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln Val Arg Ala Met Met
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Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro
 50      55      60
Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile
 65      70      75      80
Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn Cys Thr
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Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr Glu Gln
100      105      110
Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg
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Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser
145      150      155      160
Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Cys Phe Leu Glu
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Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Arg Ser Ile
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Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys Gly Lys
195      200      205
Leu Pro Ile Val Asn Glu Asp Glu Leu Val Ala Ile Ile Ala Arg
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Thr Asp Leu Lys Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys Asp Ala
225      230      235      240
Lys Lys Gln Leu Leu Cys Gly Ala Ala Ile Gly Thr His Glu Asp Asp
245      250      255
Lys Tyr Arg Leu Asp Leu Leu Ala Gln Ala Gly Val Asp Val Val Val
260      265      270
Leu Asp Ser Ser Gln Gly Asn Ser Ile Phe Gln Ile Asn Met Ile Lys
275      280      285
Tyr Ile Lys Asp Lys Tyr Pro Asn Leu Gln Val Ile Gly Gly Asn Val
290      295      300
Val Thr Ala Ala Gln Ala Lys Asn Leu Ile Asp Ala Gly Val Asp Ala
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Leu Arg Val Gly Met Gly Ser Gly Ser Ile Cys Ile Thr Gln Glu Val
325      330      335
Leu Ala Cys Gly Arg Pro Gln Ala Thr Ala Val Tyr Lys Val Ser Glu
340      345      350
Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Gly Ile Gln
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Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser Thr Val
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<300>
<301> Farazi et al.
<302> Isolation and Characterization of Mycophenolic
<303> J. Biol. Chem. (1997)
<304> 272
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Tyr	Leu	Ile	Ser	Gly	Gly	Thr	Ser	Tyr	Val	Pro	Asp	Asp	Gly	Leu	Thr	
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gca	cag	cag	ctc	ttc	aac	tgc	gga	gac	ggc	ctc	acc	tac	aat	gac	ttt	152
Ala	Gln	Gln	Leu	Phe	Asn	Cys	Gly	Asp	Gly	Leu	Thr	Tyr	Asn	Asp	Phe	
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Leu	Ile	Leu	Pro	Gly	Tyr	Ile	Asp	Phe	Thr	Ala	Asp	Gln	Val	Asp	Leu	
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Thr	Ser	Ala	Leu	Thr	Lys	Lys	Ile	Thr	Leu	Lys	Thr	Pro	Leu	Val	Ser	
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tct	ccc	atg	gac	aca	gtc	aca	gag	gct	ggg	atg	gcc	ata	gca	atg	gcg	296
Ser	Pro	Met	Asp	Thr	Val	Thr	Glu	Ala	Gly	Met	Ala	Ile	Ala	Met	Ala	
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ctt	aca	ggc	ggt	att	ggc	ttc	atc	cac	cac	aac	tgt	aca	cct	gaa	ttc	344
Leu	Thr	Gly	Gly	Ile	Gly	Phe	Ile	His	His	Asn	Cys	Thr	Pro	Glu	Phe	
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His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser Thr Val Met Met Gly
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tct ctc ctg gct gcc acc act gag gcc cct ggt gaa tac ttc ttt tcc      1256
Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly Glu Tyr Phe Phe Ser
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Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala Val Gln Asp Lys Gly
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Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln Val Arg Ala Met Met
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Glu Gly Gly Val His Ser Leu His Ser Tyr Glu Lys Arg Leu Phe
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Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala Asp Gln
                               35                               40                               45
Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro
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Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile
65                               70                               75                               80

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 Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr Glu Gln
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 Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg
 115 120 125
 Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile
 130 135 140
 Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser
 145 150 155 160
 Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Cys Phe Leu Glu
 165 170 175
 Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Arg Ser Ile
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His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala	

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	Glu Asp Ala His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys			
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	Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala			
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	Leu Ala Thr Glu Val Phe Gly Tyr Thr Ser Asn Pro Ile Gly Ile			
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	tcg ggc ggc ctg gac aag cat gct gag atc cct gat ccg ctg ttc gcg			528
	Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala			
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	atc ggt cct gcc att gtc gaa gtc ggg ggt acg aca ccc tta cca cag			576
	Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln			
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	Asp Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Ser Gln Arg Ala			
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	Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly			
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	gtg cca cca ggt agt ctt cag cct ggt aag ctt tta gct gtc caa gtg			816
	Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val			
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	Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg			
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	Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu			
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	gcc act gcc ccg ctc aca gct atc ttg agt gct gtc gtt ggc gcg gca			1008
	Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala			
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Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly	
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Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr	
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 Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys
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 <301> Natsumeda et al.
 <302> Two Distinct cDNAs for Human IMP Dehydrogenase
 <303> J. Biol. Chem. (1990)
 <304> 265
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 <302> Cloning and Sequencing of a Human cDNA coding for
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 Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr Thr Val Ser
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 Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg Glu Met
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 Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val Gly Gly Val
 325 330 335
 Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly Ala Ser Leu
 340 345 350
 Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro Val Val Gly
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<210> 21
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 <213> Homo sapien

<220>
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 <223> DHODH Truncated 39 kDa Construct

<300>

<301> Copeland, R.A., et al.
 <302> Recombinant Human Dihydroorotate Dehydrogenase
 <303> Arch. Biochem. Biophys. (1995)
 <304> 323
 <306> 79-86

<400> 21

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Met Ala Thr Gly Asp Glu Arg Phe Tyr Ala Glu His Leu Met Pro Thr	
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Leu Gln Gly Leu Leu Asp Pro Glu Ser Ala His Arg Leu Ala Val Arg	
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Phe Thr Ser Leu Gly Leu Leu Pro Arg Ala Arg Phe Gln Asp Ser Asp	
35 40 45	
atg ctg gaa gtg aga gtt ctg ggc cat aaa ttc cga aat cca gta gga	192
Met Leu Glu Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly	
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att gct gca gga ttt gac aag cat ggg gaa gcc gtg gac gga ctt tat	240
Ile Ala Ala Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr	
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Lys Met Gly Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro	
85 90 95	
cag gaa gga aac cct aga ccc aga gtc ttc cgc ctc cct gag gac caa	336
Gln Glu Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln	
100 105 110	
gct gtc att aac agg tat gga ttt aac agt cac ggg ctt tca gtg gtg	384
Ala Val Ile Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val	
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Glu His Arg Leu Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu	
130 135 140	
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Asp Gly Leu Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val	
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Asp Ala Ala Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu	
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gcc gac tac ctg gtg gtg aat gtg tcc agc ccc aac act gcc ggg ctg	576
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180 185 190	
cgg agc ctt cag gga aag gcc gag ctg cgc cgc ctg ctg acc aag gtg	624
Arg Ser Leu Gln Gly Lys Ala Glu Leu Arg Arg Leu Thr Lys Val	
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ctg cag gag agg gat ggc ttg cgg aga gtg cac agg ccg gca gtc ctg	672
Leu Gln Glu Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu	
210 215 220	

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Ser	Val	Val	Lys	Glu	Leu	Gly	Ile	Asp	Gly	Leu	Ile	Val	Thr	Asn	Thr	
				245					250					255		
acc	gtg	agt	cgc	cct	gcg	ggc	ctc	cag	ggg	gcc	ctg	cgc	tct	gaa	aca	816
Thr	Val	Ser	Arg	Pro	Ala	Gly	Leu	Gln	Gly	Ala	Leu	Arg	Ser	Glu	Thr	
			260					265					270			
gga	ggg	ctg	agt	ggg	aag	ccc	ctc	cgg	gat	tta	tca	act	caa	acc	att	864
Gly	Gly	Leu	Ser	Gly	Lys	Pro	Leu	Arg	Asp	Leu	Ser	Thr	Gln	Thr	Ile	
		275					280					285				
cgg	gag	atg	tat	gca	ctc	acc	caa	ggc	cga	gtt	ccc	ata	att	ggg	gtt	912
Arg	Glu	Met	Tyr	Ala	Leu	Thr	Gln	Gly	Arg	Val	Pro	Ile	Ile	Gly	Val	
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Gly	Gly	Val	Ser	Ser	Gly	Gln	Asp	Ala	Leu	Glu	Lys	Ile	Arg	Ala	Gly	
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gcc	tcc	ctg	gtg	cag	ctg	tac	acg	gcc	ctc	acc	ttc	tgg	ggg	cca	ccc	1008
Ala	Ser	Leu	Val	Gln	Leu	Tyr	Thr	Ala	Leu	Thr	Phe	Trp	Gly	Pro	Pro	
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gtt	gtg	ggc	aaa	gtc	aag	cgg	gaa	ctg	gag	gcc	ctt	ctg	aaa	gag	cag	1056
Val	Val	Gly	Lys	Val	Lys	Arg	Glu	Leu	Glu	Ala	Leu	Leu	Lys	Glu	Gln	
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ggc	ttt	ggc	gga	gtc	aca	gat	gcc	att	gga	gca	gat	cat	cgg	agg		1101
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 <213> Homo sapien

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 35 40 45
 Met Leu Glu Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly
 50 55 60
 Ile Ala Ala Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr
 65 70 75 80
 Lys Met Gly Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro
 85 90 95
 Gln Glu Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln
 100 105 110
 Ala Val Ile Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val
 115 120 125
 Glu His Arg Leu Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu
 130 135 140

Asp Gly Leu Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val
 145 150 155 160
 Asp Ala Ala Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu
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 Ala Asp Tyr Leu Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu
 180 185 190
 Arg Ser Leu Gln Gly Lys Ala Glu Arg Arg Leu Leu Thr Lys Val
 195 200 205
 Leu Gln Glu Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu
 210 215 220
 Val Lys Ile Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala
 225 230 235 240
 Ser Val Val Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr
 245 250 255
 Thr Val Ser Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr
 260 265 270
 Gly Gly Leu Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile
 275 280 285
 Arg Glu Met Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val
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 Gly Gly Val Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly
 305 310 315 320
 Ala Ser Leu Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro
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<210> 23
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 <223> His26Ala DHODH mutant

<300>
 <301> Davis et al.
 <302> Histidine to Alanine mutants of Human Dihydroorota
 <303> Biochem. Pharmacol. (1997)
 <304> 54
 <306> 459-465

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 Leu Gln Gly Leu Leu Asp Pro Glu Ser Ala Ala Arg Leu Ala Val Arg
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ttc acc tcc ctg ggg ctc ctt cca cgg gcc aga ttt caa gac tct gac	144
Phe Thr Ser Leu Gly Leu Leu Pro Arg Ala Arg Phe Gln Asp Ser Asp	
35 40 45	
atg ctg gaa gtg aga gtt ctg ggc cat aaa ttc cga aat cca gta gga	192
Met Leu Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly	
50 55 60	
att gct gca gga ttt gac aag cat ggg gaa gcc gtg gac gga ctt tat	240
Ile Ala Ala Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr	
65 70 75	
aag atg ggc ttt ggt ttt gtt gag ata gga agt gtg act cca aaa cct	288
Lys Met Gly Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro	
80 85 90 95	
cag gaa gga aac cct aga ccc aga gtc ttc cgc ctc cct gag gac caa	336
Gln Glu Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln	
100 105 110	
gct gtc att aac agg tat gga ttt aac agt cac ggg ctt tca gtg gtg	384
Ala Val Ile Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val	
115 120 125	
gaa cac agg tta cgg gcc aga cag cag aag cag gcc aag ctc aca gaa	432
Glu His Arg Leu Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu	
130 135 140	
gat gga ctg cct ctg ggg gtc aac ttg ggg aag aac aag acc tca gtg	480
Asp Gly Leu Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val	
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Asp Ala Ala Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu	
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Ala Asp Tyr Leu Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu	
180 185 190	
cgg agc ctt cag gga aag gcc gag ctg cgc cgc ctg ctg acc aag gtg	624
Arg Ser Leu Gln Gly Lys Ala Glu Leu Arg Arg Leu Leu Thr Lys Val	
195 200 205	
ctg cag gag agg gat ggc ttg cgg aga gtg cac agg ccg gca gtc ctg	672
Leu Gln Glu Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu	
210 215 220	
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Val Lys Ile Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala	
225 230 235	
agt gtg gtc aaa gag ttg ggc atc gat ggg ctg att gtt acg aac acc	768
Ser Val Val Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr	
240 245 250 255	
acc gtg agt cgc cct gcg ggc ctc cag ggt gcc ctg cgc tct gaa aca	816
Thr Val Ser Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr	
260 265 270	
gga ggg ctg agt ggg aag ccc ctc cgg gat tta tca act caa acc att	864

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ggt	ggt	gtg	agc	agc	ggg	cag	gac	gcg	ctg	gag	aag	atc	cgg	gca	ggg	960	
Gly	Gly	Val	Ser	Ser	Gly	Gln	Asp	Ala	Leu	Glu	Lys	Ile	Arg	Ala	Gly		
		305				310					315						
gcc	tcc	ctg	gtg	cag	ctg	tac	acg	gcc	ctc	acc	ttc	tgg	ggg	cca	ccc	1008	
Ala	Ser	Leu	Val	Gln	Leu	Tyr	Thr	Ala	Leu	Thr	Phe	Trp	Gly	Pro	Pro		
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 <213> Homo sapien

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 35 40 45
 Leu Glu Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly Ile
 50 55 60
 Ala Ala Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr Lys
 65 70 75 80
 Met Gly Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro Gln
 85 90 95
 Glu Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln Ala
 100 105 110
 Val Ile Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val Glu
 115 120 125
 His Arg Leu Arg Ala Arg Gln Lys Gln Ala Lys Leu Thr Glu Asp
 130 135 140
 Gly Leu Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val Asp
 145 150 155 160
 Ala Ala Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu Ala
 165 170 175
 Asp Tyr Leu Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu Arg
 180 185 190
 Ser Leu Gln Gly Lys Ala Glu Leu Arg Arg Leu Leu Thr Lys Val Leu
 195 200 205
 Gln Glu Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu Val
 210 215 220
 Lys Ile Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala Ser
 225 230 235 240
 Val Val Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr Thr
 245 250 255

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Val Ser Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr Gly
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Gly Leu Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg
      275      280      285
Glu Met Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val Gly
      290      295      300
Gly Val Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly Ala
      305      310      315      320
Ser Leu Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro Val
      325      330      335
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Phe Gly Gly Val Thr Asp Ala Ile Gly Ala Asp His Arg Arg
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<210> 25

<211> 1560

<212> DNA

<213> Aspergillus nidulans

<220>

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<222> (1)...(1560)

<223> Aspergillus nidulans Val200Glu mutant DHODH cDNA

<221> mutation

<222> 599

<223> T to A mutataction

<400> 25

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ctg ggt ggt tgt cgc cgt ctc cca cta acc tgc aga caa ctt cga ttc      96
Leu Gly Gly Cys Arg Arg Leu Pro Leu Thr Cys Arg Gln Leu Arg Phe
          20          25          30

gcc tcc gac agc gga gcc gca gcg gca act aca aaa gca acg gcc gaa      144
Ala Ser Asp Ser Gly Ala Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu
          35          40          45

tca gca gcc gag tca gct agt ata aac gtc aaa gag gca ccc aaa aag      192
Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys
          50          55          60

gcc gga cgg ggc ctg cgg cgc acg gtc ctg gga acg tgc ttg gcg ctg      240
Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Gly Thr Ser Leu Ala Leu
          65          70          75          80

acg ctg ctg gtt gga tat gtc tac ggg acg gac acc cgg gcg agt gtg      288
Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val
          85          90          95

cat cgg tac ggt gtt gtg cgg ctg att aga gca ttg tat cct gat gcg      336
His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala
          100          105          110

gaa gat gcg cat cat att ggt gtc gat act tta aag atg ctg tat aag      384
Glu Asp Ala His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys
          115          120          125

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tat ggt ctg cat cca agg gaa cgg ggg gat ccg gat gga gat ggg gcg Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala 130 135 140	432
ctg gcg aca gag gtc ttt ggg tat aca ctg tca aac cca att ggc ata Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile 145 150 155 160	480
tcg ggc ggc ctg gac aag cat gct gag atc cct gat ccg ctg ttc gcg Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala 165 170 175	528
atc ggt cct gcc att gtc gaa gtc ggg ggt acg aca ccc tta cca cag Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln 180 185 190	576
gat ggt aac ccg cgt cct cgc gaa ttc cga ctt cca tca cag aga gcg Asp Gly Asn Pro Arg Pro Arg Glu Phe Arg Leu Pro Ser Gln Arg Ala 195 200 205	624
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gca acg ttg aaa gaa acc ggc ggg tat tca ggt cca cag ctg ttc gat			1248
Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp			
	405	410	415
cgc aca gtg gcc ctt gtg gct cgg tac cgc tcc atg ctg gat gcg gag			1296
Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu			
	420	425	430
tcg gaa acg gcc gga tcc gcc aag gat tca gca gcg acc ata gcg caa			1344
Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln			
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aca gag cca ggc tcg gaa aac gtt cct cct gtg gaa gcg cca agc gga			1392
Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly			
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ctg ccg cgc aaa gtt atc ttc gct tcg ggt ggt atc acc aac ggg aag			1440
Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys			
	465	470	475
cag gct cac gct gtt tta gac aca ggg gca tct gtt gcc atg atg tac			1488
Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr			
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acc ggt gtg gtc tat ggt ggc gtc ggc act gtc act cga gtg aag caa			1536
Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln			
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<211> 520

<212> PRT

<213> Aspergillus nidulans

<400> 26

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Ser	Ala	Ala	Glu	Ser	Ala	Ser	Ile	Asn	Val	Lys	Glu	Ala	Pro	Lys	Lys
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His	Arg	Tyr	Gly	Val	Val	Pro	Leu	Ile	Arg	Ala	Leu	Tyr	Pro	Asp	Ala
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Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala		
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Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln		
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Asp Gly Asn Pro Arg Pro Arg Glu Phe Arg Leu Pro Ser Gln Arg Ala		
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Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly		
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Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val		
	260	265
Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg		
	275	280
Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu		
	290	295
Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln		
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Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala		
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Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser		
	340	345
Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val		
	355	360
Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg		
	370	375
Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln		
385	390	395
Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp		
	405	410
Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu		
	420	425
Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln		
	435	440
Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly		
	450	455
Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys		
465	470	475
Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr		
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Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln		
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Glu Leu Arg Thr Ala Lys Lys Glu		
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<210> 27

<211> 1560

<212> DNA

<213> Aspergillus nidulans

<220>

<221> CDS

<222> (1)...(1560)

<223> Aspergillus nidulans Alal15Val mutant DHODH cDNA

<221> mutation

<222> 344

<223> C to T mutation

<400> 27

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Met Ala Thr Asn Ser Phe Arg Lys Leu Thr Phe Ser Gly Ala Ser Arg	
1 5 10 15	
ctg ggt ggt tgt cgc cgt ctc cca cta acc tgc aga caa ctt cga ttc	96
Leu Gly Gly Cys Arg Arg Leu Pro Leu Thr Cys Arg Gln Leu Arg Phe	
20 25 30	
gcc tcc gac agc gga gcc gca gcg gca act aca aaa gca acg gcc gaa	144
Ala Ser Asp Ser Gly Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu	
35 40 45	
tca gca gcc gag tca gct agt ata aac gtc aaa gag gca ccc aaa aag	192
Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys	
50 55 60	
gcc gga cgg ggc ctg cgg cgc acg gtc ctg gga acg tcg ttg gcg ctg	240
Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Thr Ser Leu Ala Leu	
65 70 75 80	
acg ctg ctg gtt gga tat gtc tac ggg acg gac acc cgg gcg agt gtg	288
Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val	
85 90 95	
cat cgg tac ggt gtt gtg ccg ctg att aga gca ttg tat cct gat gcg	336
His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala	
100 105 110	
gaa gat gtg cat cat att ggt gtc gat act tta aag atg ctg tat aag	384
Glu Asp Val His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys	
115 120 125	
tat ggt ctg cat cca agg gaa cgg ggg gat ccg gat gga gat ggg gcg	432
Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala	
130 135 140	
ctg gcg aca gag gtc ttt ggg tat aca ctg tca aac cca att ggc ata	480
Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile	
145 150 155 160	
tcg ggc ggc ctg gac aag cat gct gag atc cct gat ccg ctg ttc gcg	528
Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala	
165 170 175	
atc ggt cct gcc att gtc gaa gtc ggg ggt acg aca ccc tta cca cag	576
Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln	
180 185 190	
gat ggt aac ccg cgt cct cgc gta ttc cga ctt cca tca cag aga gcg	624
Asp Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Ser Gln Arg Ala	
195 200 205	
atg ata aac cgg tac ggc ctc aac tcc aaa ggc gca gat cac atg gca	672
Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala	
210 215 220	
gct atc ttg gag caa cga gta cgc gat ttt gcc tac gca aac gga ttt	720
Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe	
225 230 235 240	

ggg gca tac gat gcg gct aag cag cgt gta ttg gac ggc gaa gct ggt	768
Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly	
245 250 255	
gtg cca cca ggt agt ctt cag cct ggt aag ctt tta gct gtc caa gtg	816
Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val	
260 265 270	
gca aag aac aag gcc act cct gac ggc gac att gaa gcc atc aag cgc	864
Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg	
275 280 285	
gac tat gtg tat tgc gtg gac cgt gtg gcc aaa tac gct gat att ctt	912
Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu	
290 295 300	
gtt gtg aat gta tcg agc ccc aac aca ccc ggt ctc cgt gac ctt caa	960
Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln	
305 310 315 320	
gcc act gcc ccg ctc aca gct atc ttg agt gct gtc gtt ggc gcg gca	1008
Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala	
325 330 335	
aag agc gtg aac cgc aag acc aaa cca tat gtt atg gtc aag gtc agt	1056
Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser	
340 345 350	
ccg gat gaa gac tca gat gaa caa gtc tct ggt atc tgc gac gcc gtc	1104
Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val	
355 360 365	
cga gca tcc ggt gtc gac gga gtg att gtc gga aac aca aca aac cgt	1152
Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg	
370 375 380	
cgc ccc gac cct ata ccc caa ggt tac act ctt ccg gcc aag gag cag	1200
Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln	
385 390 395 400	
gca acg ttg aaa gaa acc ggc ggg tat tca ggt cca cag ctg ttc gat	1248
Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp	
405 410 415	
cgc aca gtg gcc ctt gtg gct cgg tac cgc tcc atg ctg gat gcg gag	1296
Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu	
420 425 430	
tcg gaa acg gcc gga tcc gcc aag gat tca gca gcg acc ata gcg caa	1344
Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln	
435 440 445	
aca gag cca ggc tcg gaa aac gtt cct cct gtg gaa gcg cca agc gga	1392
Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly	
450 455 460	
ctg ccg cgc aaa gtt atc ttc gct tcg ggt ggt atc acc aac ggg aag	1440
Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys	
465 470 475 480	
cag gct cac gct gtt tta gac aca ggg gca tct gtt gcc atg atg tac	1488

Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr
 485 490 495

acc ggt gtg gtc tat ggt ggc gtc ggc act gtc act cga gtg aag caa 1536
 Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln
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gaa ctt cga acg gcg aaa aag gag 1560
 Glu Leu Arg Thr Ala Lys Lys Glu
 515 520

<210> 28
 <211> 520
 <212> PRT
 <213> Aspergillus nidulans

<400> 28
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 35 40 45
 Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys
 50 55 60
 Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Gly Thr Ser Leu Ala Leu
 65 70 75 80
 Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val
 85 90 95
 His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala
 100 105 110
 Glu Asp Val His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys
 115 120 125
 Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala
 130 135 140
 Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile
 145 150 155 160
 Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala
 165 170 175
 Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln
 180 185 190
 Asp Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Ser Gln Arg Ala
 195 200 205
 Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala
 210 215 220
 Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe
 225 230 235 240
 Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly
 245 250 255
 Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val
 260 265 270
 Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg
 275 280 285
 Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu
 290 295 300
 Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln
 305 310 315 320
 Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala
 325 330 335
 Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser
 340 345 350

Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val
 355 360 365
 Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg
 370 375 380
 Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln
 385 390 395 400
 Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp
 405 410 415
 Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu
 420 425 430
 Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln
 435 440 445
 Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly
 450 455 460
 Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys
 465 470 475 480
 Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr
 485 490 495
 Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln
 500 505 510
 Glu Leu Arg Thr Ala Lys Lys Glu
 515 520

<210> 29

<211> 1707

<212> DNA

<213> Mus musculus

<220>

<221> CDS

<222> (67)...(1611)

<223> wild-type IMP dehydrogenase cDNA

<400> 29

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 gtgggtc atg gcg gac tac ctg att agc gga ggc acc tct tac gtg ccg 108
 Met Ala Asp Tyr Leu Ile Ser Gly Gly Thr Ser Tyr Val Pro

1

5

10

gac gac ggg ctc aca gcg cag cag ctc ttc aac tgc ggg gac ggc ctc 156
 Asp Asp Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu
 15 20 25 30

acc tac aat gat ttt ctc att ctt cct ggg tat atc gac ttc act gca 204
 Thr Tyr Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala
 35 40 45

gat cag gtg gac ttg acg tct gct cta act aag aag att aca cta aag 252
 Asp Gln Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys
 50 55 60

acc cca ttg gtt tcc tca ccc atg gac act gtc aca gag gct gga atg 300
 Thr Pro Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met
 65 70 75

gcc atc gcg atg gcg ctt aca gga ggt att ggt ttc atc cac cac aac 348
 Ala Ile Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn
 80 85 90

tgc aca cct gaa ttc cag gcc aat gaa gtt cgg aaa gtg aag aaa tac 396
 Cys Thr Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr
 95 100 105 110

gaa	cag	gga	ttc	atc	act	gac	ccc	gtg	gtc	ctt	agc	ccc	aag	gat	cgt	444
Glu	Gln	Gly	Phe	Ile	Thr	Asp	Pro	Val	Val	Leu	Ser	Pro	Lys	Asp	Arg	
				115					120					125		
gta	cgc	gat	gtt	ttt	gag	gcc	aaa	gcc	agg	cat	ggc	ttc	tgt	ggg	atc	492
Val	Arg	Asp	Val	Phe	Glu	Ala	Lys	Ala	Arg	His	Gly	Phe	Cys	Gly	Ile	
			130					135					140			
ccc	atc	aca	gat	aca	ggc	cgg	atg	ggg	agt	cga	ttg	gtg	ggc	atc	atc	540
Pro	Ile	Thr	Asp	Thr	Gly	Arg	Met	Gly	Ser	Arg	Leu	Val	Gly	Ile	Ile	
		145					150					155				
tcc	tca	agg	gac	att	gat	ttc	ctc	aag	gag	gaa	gag	cat	gac	cgg	ttc	588
Ser	Ser	Arg	Asp	Ile	Asp	Phe	Leu	Lys	Glu	Glu	Glu	His	Asp	Arg	Phe	
	160					165					170					
ttg	gaa	gag	atc	atg	act	aag	agg	gaa	gat	ttg	gtg	gtc	gcc	cct	gcc	636
Leu	Glu	Glu	Ile	Met	Thr	Lys	Arg	Glu	Asp	Leu	Val	Val	Ala	Pro	Ala	
175					180				185						190	
ggc	gtc	act	ctg	aaa	gag	gca	aat	gag	att	ctg	cag	cga	agt	aaa	aag	684
Gly	Val	Thr	Leu	Lys	Glu	Ala	Asn	Glu	Ile	Leu	Gln	Arg	Ser	Lys	Lys	
				195					200					205		
gga	aag	ttg	ccc	att	gtg	aat	gaa	aat	gat	gag	ctg	gta	gcc	atc	att	732
Gly	Lys	Leu	Pro	Ile	Val	Asn	Glu	Asn	Asp	Glu	Leu	Val	Ala	Ile	Ile	
			210					215					220			
gcc	cgg	aca	gac	cta	aag	aag	aat	cgt	gat	tac	ccc	ctg	gcc	tcc	aaa	780
Ala	Arg	Thr	Asp	Leu	Lys	Lys	Asn	Arg	Asp	Tyr	Pro	Leu	Ala	Ser	Lys	
		225					230					235				
gat	gcc	aag	aag	caa	ctg	ctg	tgt	ggg	gca	gcc	att	ggc	act	cat	gag	828
Asp	Ala	Lys	Lys	Gln	Leu	Leu	Cys	Gly	Ala	Ala	Ile	Gly	Thr	His	Glu	
	240					245					250					
gat	gac	aag	tat	agg	ctg	gac	tta	ctg	gcc	ctt	gct	ggg	gtg	gat	gta	876
Asp	Asp	Lys	Tyr	Arg	Leu	Asp	Leu	Leu	Ala	Leu	Ala	Gly	Val	Asp	Val	
	255				260					265					270	
gtg	gtt	ttg	gac	tct	tcc	cag	gga	aac	tcc	atc	ttc	caa	atc	aat	atg	924
Val	Val	Leu	Asp	Ser	Ser	Gln	Gly	Asn	Ser	Ile	Phe	Gln	Ile	Asn	Met	
				275					280					285		
atc	aaa	tac	atc	aag	gag	aag	tat	ccc	agt	cta	cag	gtc	att	gga	ggc	972
Ile	Lys	Tyr	Ile	Lys	Glu	Lys	Tyr	Pro	Ser	Leu	Gln	Val	Ile	Gly	Gly	
			290					295					300			
aat	gta	gtc	act	gct	gcg	caa	gcc	aag	aac	ctc	ata	gat	gca	ggg	gta	1020
Asn	Val	Val	Thr	Ala	Ala	Gln	Ala	Lys	Asn	Leu	Ile	Asp	Ala	Gly	Val	
		305					310					315				
gat	gct	ttg	cga	gtc	ggc	atg	gga	agt	ggg	tcc	atc	tgc	atc	acc	cag	1068
Asp	Ala	Leu	Arg	Val	Gly	Met	Gly	Ser	Gly	Ser	Ile	Cys	Ile	Thr	Gln	
	320					325					330					
gaa	gtg	ttg	gcc	tgt	ggg	cgg	ccc	caa	gcc	aca	gca	gtg	tac	aag	gtc	1116
Glu	Val	Leu	Ala	Cys	Gly	Arg	Pro	Gln	Ala	Thr	Ala	Val	Tyr	Lys	Val	
335					340					345					350	
tct	gag	tat	gcc	cgt	cgc	ttt	ggg	gtt	cct	gtt	att	gct	gat	gga	gga	1164

Ser Glu Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Gly
 355 360 365

atc caa aat gtg ggt cat att gcc aaa gct ttg gct ctt ggg gct tcc 1212
 Ile Gln Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser
 370 375 380

aca gtc atg atg ggc tcc ctc ctg gct gcc acc act gag gcc cct ggc 1260
 Thr Val Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly
 385 390 395

gag tac ttc ttc tca gat ggg atc cgg ctg aag aaa tac cga ggt atg 1308
 Glu Tyr Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met
 400 405 410

ggt tct ctt gat gcc atg gac aaa cat ctc agc agc cag aac cga tac 1356
 Gly Ser Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr
 415 420 425 430

ttc agt gaa gct gac aaa atc aaa gtg gcc caa gga gtt tca ggg gca 1404
 Phe Ser Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala
 435 440 445

gtg cag gac aag ggg tct atc cac aag ttc gtt cct tac ctg att gct 1452
 Val Gln Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala
 450 455 460

ggc atc cag cat tcc tgt caa gac att ggt gcc aag agt tta acc caa 1500
 Gly Ile Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln
 465 470 475

gtc aga gcc atg acg tac tcg ggg gag ctt aaa ttt gag aag agg aca 1548
 Val Arg Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr
 480 485 490

tcc tct gct cag gtg gaa ggt ggc gtc cac agc ctc cat tcg tac gag 1596
 Ser Ser Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu
 495 500 505 510

aaa cgg ctt ttc tga aaacagatcc agtatatgcc ttgaattttt caataaaagt 1651
 Lys Arg Leu Phe *

ttgggaaaaaa aaaagtga aaacagatcc agtatatgcc ttgaattttt caataaaagt 1707

<210> 30

<211> 514

<212> PRT

<213> Mus musculus

<400> 30

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 Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu Thr Tyr
 20 25 30
 Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala Asp Gln
 35 40 45
 Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro
 50 55 60
 Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile
 65 70 75 80
 Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn Cys Thr

Pro	Glu	Phe	Gln	85	Asn	Glu	Val	Arg	90	Lys	Val	Lys	Lys	Tyr	95	Glu	Gln
			100	Asp	Pro	Val	Val	Leu	105	Ser	Pro	Lys	Asp	Arg	110	Val	Arg
Gly	Phe	Ile	Thr	115				120	120	His	Gly	Phe	Cys	Gly	125	Ile	Pro
Asp	Val	Phe	Glu	Ala	Lys	Ala	Arg	His	135	Arg	Leu	Val	Gly	Ile	140	Ile	Ser
Thr	130	Asp	Thr	Gly	Arg	Met	Gly	Ser	150	Arg	Leu	Val	Gly	Ile	155	Ile	Ser
145						150											160
Arg	Asp	Ile	Asp	Phe	Leu	Lys	Glu	Glu	170	His	Asp	Arg	Phe	Leu	175	Glu	
				165													
Glu	Ile	Met	Thr	Lys	Arg	Glu	Asp	Leu	185	Val	Val	Ala	Pro	Ala	190	Gly	Val
Thr	195	Leu	Lys	Glu	Ala	Asn	Glu	Ile	200	Leu	Gln	Arg	Ser	Lys	205	Lys	Gly
Leu	210	Pro	Ile	Val	Asn	Glu	Asn	Asp	215	Glu	Leu	Val	Ala	Ile	220	Ile	Ala
Thr	225	Asp	Leu	Lys	Lys	Asn	Arg	Asp	230	Tyr	Pro	Leu	Ala	Ser	235	Lys	Asp
Lys	Lys	Gln	Leu	Leu	Cys	Gly	Ala	Ala	245	Ile	Gly	Thr	His	Glu	250	Asp	Ala
				245													
Lys	Tyr	Arg	Leu	Asp	Leu	Leu	Ala	Leu	260	Ala	Gly	Val	Asp	Val	265	Val	Val
Leu	275	Asp	Ser	Ser	Gln	Gly	Asn	Ser	280	Ile	Phe	Gln	Ile	Asn	285	Met	Ile
Tyr	290	Ile	Lys	Glu	Lys	Tyr	Pro	Ser	295	Leu	Gln	Val	Ile	Gly	300	Gly	Asn
Val	305	Thr	Ala	Ala	Gln	Ala	Lys	Asn	310	Leu	Ile	Asp	Ala	Gly	315	Val	Asp
Leu	325	Arg	Val	Gly	Met	Gly	Ser	Gly	330	Ser	Ile	Cys	Ile	Thr	335	Gln	Glu
Leu	340	Ala	Cys	Gly	Arg	Pro	Gln	Ala	345	Thr	Ala	Val	Tyr	Lys	350	Val	Ser
Tyr	355	Ala	Arg	Arg	Phe	Gly	Val	Pro	360	Val	Ile	Ala	Asp	Gly	365	Gly	Ile
Asn	370	Val	Gly	His	Ile	Ala	Lys	Ala	375	Leu	Ala	Leu	Gly	Ala	380	Ser	Thr
Met	385	Met	Gly	Ser	Leu	Leu	Ala	Ala	390	Thr	Thr	Glu	Ala	Pro	395	Gly	Glu
Phe	405	Phe	Ser	Asp	Gly	Ile	Arg	Leu	410	Lys	Lys	Tyr	Arg	Gly	415	Met	Gly
Leu	420	Asp	Ala	Met	Asp	Lys	His	Leu	425	Ser	Ser	Gln	Asn	Arg	430	Tyr	Phe
Glu	435	Ala	Asp	Lys	Ile	Lys	Val	Ala	440	Gln	Gly	Val	Ser	Gly	445	Ala	Val
Asp	450	Lys	Gly	Ser	Ile	His	Lys	Phe	455	Val	Pro	Tyr	Leu	Ile	460	Ala	Gly
Gln	465	His	Ser	Cys	Gln	Asp	Ile	Gly	470	Ala	Lys	Ser	Leu	Thr	475	Gln	Val
Ala	485	Met	Thr	Tyr	Ser	Gly	Glu	Leu	490	Lys	Phe	Glu	Lys	Arg	495	Thr	Ser
Ala	500	Gln	Val	Glu	Gly	Gly	Val	His	505	Ser	Leu	His	Ser	Tyr	510	Glu	Lys
Leu		Phe															

<210> 31

<211> 1707

<212> DNA

<213> Mus musculus

<220>

<221> CDS
 <222> (67)...(1611)
 <223> mouse IMP dehydrogenase cDNA double mutant:
 Thr333Ile
 Ser351Tyr

<221> mutation
 <222> 1064
 <223> C to T mutation

<221> mutation
 <222> 1118
 <223> C to A mutation

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 Met Ala Asp Tyr Leu Ile Ser Gly Gly Thr Ser Tyr Val Pro
 1 5 10

gac gac ggg ctc aca gcg cag cag ctc ttc aac tgc ggg gac ggc ctc 156
 Asp Asp Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu
 15 20 25 30

acc tac aat gat ttt ctc att ctt cct ggg tat atc gac ttc act gca 204
 Thr Tyr Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala
 35 40 45

gat cag gtg gac ttg acg tct gct cta act aag aag att aca cta aag 252
 Asp Gln Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys
 50 55 60

acc cca ttg gtt tcc tca ccc atg gac act gtc aca gag gct gga atg 300
 Thr Pro Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met
 65 70 75

gcc atc gcg atg gcg ctt aca gga ggt att ggt ttc atc cac cac aac 348
 Ala Ile Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn
 80 85 90

tgc aca cct gaa ttc cag gcc aat gaa gtt cgg aaa gtg aag aaa tac 396
 Cys Thr Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr
 95 100 105 110

gaa cag gga ttc atc act gac ccc gtg gtc ctt agc ccc aag gat cgt 444
 Glu Gln Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg
 115 120 125

gta cgc gat gtt ttt gag gcc aaa gcc agg cat ggc ttc tgt ggt atc 492
 Val Arg Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile
 130 135 140

ccc atc aca gat aca ggc cgg atg ggg agt cga ttg gtg ggc atc atc 540
 Pro Ile Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile
 145 150 155

tcc tca agg gac att gat ttc ctc aag gag gaa gag cat gac cgg ttc 588
 Ser Ser Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Arg Phe
 160 165 170

ttg gaa gag atc atg act aag agg gaa gat ttg gtg gtc gcc cct gcc 636
 Leu Glu Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala

175	180	185	190	
ggc gtc act ctg aaa gag gca aat gag att ctg cag cga agt aaa aag Gly Val Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys 195 200 205				684
gga aag ttg ccc att gtg aat gaa aat gat gag ctg gta gcc atc att Gly Lys Leu Pro Ile Val Asn Glu Asn Asp Glu Leu Val Ala Ile Ile 210 215 220				732
gcc cgg aca gac cta aag aag aat cgt gat tac ccc ctg gcc tcc aaa Ala Arg Thr Asp Leu Lys Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys 225 230 235				780
gat gcc aag aag caa ctg ctg tgt ggg gca gcc att ggc act cat gag Asp Ala Lys Lys Gln Leu Cys Gly Ala Ala Ile Gly Thr His Glu 240 245 250				828
gat gac aag tat agg ctg gac tta ctg gcc ctt gct ggt gtg gat gta Asp Asp Lys Tyr Arg Leu Asp Leu Leu Ala Leu Ala Gly Val Asp Val 255 260 265 270				876
gtg gtt ttg gac tct tcc cag gga aac tcc atc ttc caa atc aat atg Val Val Leu Asp Ser Ser Gln Gly Asn Ser Ile Phe Gln Ile Asn Met 275 280 285				924
atc aaa tac atc aag gag aag tat ccc agt cta cag gtc att gga ggc Ile Lys Tyr Ile Lys Glu Lys Tyr Pro Ser Leu Gln Val Ile Gly Gly 290 295 300				972
aat gta gtc act gct gcg caa gcc aag aac ctc ata gat gca ggt gta Asn Val Val Thr Ala Ala Gln Ala Lys Asn Leu Ile Asp Ala Gly Val 305 310 315				1020
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gaa gtg ttg gcc tgt ggg cgg ccc caa gcc aca gca gtg tac aag gtc Glu Val Leu Ala Cys Gly Arg Pro Gln Ala Thr Ala Val Tyr Lys Val 335 340 345 350				1116
tat gag tat gcc cgt cgc ttt ggt gtt cct gtt att gct gat gga gga Tyr Glu Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Gly 355 360 365				1164
atc caa aat gtg ggt cat att gcc aaa gct ttg gct ctt ggg gct tcc Ile Gln Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser 370 375 380				1212
aca gtc atg atg ggc tcc ctc ctg gct gcc acc act gag gcc cct ggc Thr Val Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly 385 390 395				1260
gag tac ttc ttc tca gat ggg atc cgg ctg aag aaa tac cga ggt atg Glu Tyr Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met 400 405 410				1308
ggt tct ctt gat gcc atg gac aaa cat ctc agc agc cag aac cga tac Gly Ser Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr 415 420 425 430				1356

ttc agt gaa gct gac aaa atc aaa gtg gcc caa gga gtt tca ggg gca 1404
 Phe Ser Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala
 435 440 445
 gtg cag gac aag ggg tct atc cac aag ttc gtt cct tac ctg att gct 1452
 Val Gln Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala
 450 455 460
 ggc atc cag cat tcc tgt caa gac att ggt gcc aag agt tta acc caa 1500
 Gly Ile Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln
 465 470 475
 gtc aga gcc atg acg tac tcg ggg gag ctt aaa ttt gag aag agg aca 1548
 Val Arg Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr
 480 485 490
 tcc tct gct cag gtg gaa ggt ggc gtc cac agc ctc cat tcg tac gag 1596
 Ser Ser Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu
 495 500 505 510
 aaa cgg ctt ttc tga aaacagatcc agtatatgcc ttgaattttt caataaaagt 1651
 Lys Arg Leu Phe *

ttgggaaaaa aaaagtgaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 1707

<210> 32
 <211> 514
 <212> PRT
 <213> Mus musculus

<400> 32
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 Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu Thr Tyr
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 Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala Asp Gln
 35 40 45
 Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro
 50 55 60
 Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile
 65 70 75 80
 Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn Cys Thr
 85 90 95
 Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr Glu Gln
 100 105 110
 Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg
 115 120 125
 Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile
 130 135 140
 Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser
 145 150 155 160
 Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Arg Phe Leu Glu
 165 170 175
 Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala Gly Val
 180 185 190
 Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys Gly Lys
 195 200 205
 Leu Pro Ile Val Asn Glu Asn Asp Glu Leu Val Ala Ile Ile Ala Arg
 210 215 220
 Thr Asp Leu Lys Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys Asp Ala
 225 230 235 240

Lys Lys Gln Leu Leu Cys Gly Ala Ala Ile Gly Thr His Glu Asp Asp
 245 250 255
 Lys Tyr Arg Leu Asp Leu Leu Ala Leu Ala Gly Val Asp Val Val Val
 260 265 270
 Leu Asp Ser Ser Gln Gly Asn Ser Ile Phe Gln Ile Asn Met Ile Lys
 275 280 285
 Tyr Ile Lys Glu Lys Tyr Pro Ser Leu Gln Val Ile Gly Gly Asn Val
 290 295 300
 Val Thr Ala Ala Gln Ala Lys Asn Leu Ile Asp Ala Gly Val Asp Ala
 305 310 315 320
 Leu Arg Val Gly Met Gly Ser Gly Ser Ile Cys Ile Ile Gln Glu Val
 325 330 335
 Leu Ala Cys Gly Arg Pro Gln Ala Thr Ala Val Tyr Lys Val Tyr Glu
 340 345 350
 Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Ile Gln
 355 360 365
 Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser Thr Val
 370 375 380
 Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly Glu Tyr
 385 390 395 400
 Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met Gly Ser
 405 410 415
 Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr Phe Ser
 420 425 430
 Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala Val Gln
 435 440 445
 Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala Gly Ile
 450 455 460
 Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln Val Arg
 465 470 475 480
 Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr Ser Ser
 485 490 495
 Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu Lys Arg
 500 505 510
 Leu Phe

<210> 33
 <211> 5627
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Sequence of pMG
 plasmid from InvivoGen

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 tttgtgatgc tattgcttta tttgtgaaat ttgtgatgct attgctttat ttgtaaccat 180
 tataagctgc aataaacaag ttaacaacaa caattgcatt catTTTTatgt ttcaggttca 240
 ggggggaggtg tgggaggttt tttaaagcaa gtaaaacctc tacaaatgtg gtagatccat 300
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 agggacacgt cgactactaa

<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Forward primer for amplification-based cloning of hIMPDH type II cDNA

<400> 34
gctatctgca ggccgccacc atggccgact acctgattag 40

<210> 35
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Reverse primer for amplification-based cloning of hIMPDH type II cDNA

<400> 35
catactcttc gccgaaaaga ctagatctcg atc 33

<210> 36
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Forward primer for T333I mutation of hIMPDH type II cDNA

<400> 36
ggctccatct gcattatcca ggaagtgctg gc 32

<210> 37
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Reverse primer for T333I mutation of hIMPDH type II cDNA

<400> 37
ccgaggtaga cgtaataggt ccttcacgac cg 32

<210> 38
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Forward primer for S351Y mutation of hIMPDH type II cDNA

<400> 38

cagcagtgtgta caaggtgtat gagtatgcac ggcgcttt

38

<210> 39

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Reverse primer for S351Y mutation of hIMPDPH type II cDNA

<400> 39

gtcgtcacat gttccacata ctcatacgtg ccgcgaaac

39